August 20, 1999

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Docket No. 99N-1737

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Dear Sir or Madam:

TCI is submitting two copies of these comments in response to the June 22, 1999 Federal Register (FR) notice requesting input on the feasibility of including information on device investigations for serious or life threatening conditions in a public data bank. TCI is opposed to this public disclosure of information which was previously held confidential by the Agency. Our opposition is based on the adverse risk to public health that such a data bank may entail, and the incentive such a data bank would create to conduct clinical trials outside the United States.

In the FR notice, the Agency stated eight general issues for which it is requesting public comment. The questions focused on the logistics and risks of implementing the proposed data bank, but failed to present the global issue. TCI believes that the first question to ask is "what need is currently not being met?" The disclosure of device trial data to the general public has no inherent benefit unless the public can affect the trial progress. This affect could be as little as increasing the pool of potential patients presented for screening, or as significant as altering the trial population sufficiently to void any outcome. The implication that a patient may benefit by being enrolled into these types of trials must be offset by the realization that this same patient may be harmed by his/her enrollment. If the purpose of disclosure is to make a benefit more readily available to the public, then the "benefit" must be clearly defined.

Is there a benefit to a patient with a serious or life threatening condition in being enrolled into a device trial? The answer of course is that any benefit is unknown, but potential benefits may be postulated. Good clinical practice requires that a known benefit should be made available to any suitable patient. Withholding known beneficial therapies is inappropriate. If a benefit is known to exist then the purpose of the trial must be brought into question. Therefore, clinical trials of devices to treat these serious conditions must be done only when the benefit is not known. Indeed the primary purpose of an IDE trial is to *establish* the safety and efficacy of the device. Claiming or implying an unproven benefit is prohibited. A risk comes from the implication that a government "sponsored" data bank implies some level of safety, yet none can be claimed.

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Without a clear benefit to wide publication of the existence of device clinical trials, TCI is concerned that a public health risk may be created by this data bank. This risk comes from the increased likelihood that patients will have access to information that allows them to falsely meet the enrollment criteria. Patients are currently screened for enrollment in these trials by trained health care professionals. If the patient can "self diagnose" their eligibility for a trial, they will be able to use this knowledge when they present themselves for enrollment. The risk to their health comes from the incentive to alter their current prescribed treatment(s). For example, if a study requires that patients not take a particular medication in order to qualify, a patient seeking to be enrolled may stop his/her medication just to qualify. The potential patient can further increase their chance of this deception being missed by "shopping" for a site willing to enroll them from among all the sites listed in the database. This self diagnosis and treatment is a public health risk that is controlled in current device trials by the screening of patients in a very regulated manner.

These same patients are very adept at pressuring clinicians to use the experimental device outside the scope of the trial. With serious and life threatening conditions creating the urgency, patients have a strong incentive to push for the treatment. The clinicians can thwart much of this pressure by explaining the risks associated with the device. However, the patients often have the perception that a trial would not be underway unless the potential benefits outweigh the risks. These patients can be better protected and still provided with unapproved devices through application of either the emergency use process or the treatment use IDE process.

Will the Agency allow sponsors to enroll more patients if the data bank increases demand? If the number of patients is set by the statistical rationale for the hypothesis being tested, then increasing the demand only increases the likelihood of pressure on the investigational sites to perform deviations from the protocol or apply emergency use criteria.

Another issue the Agency must consider in reviewing a potential data bank is; "are clinical investigations of medical devices in the United States not being completed due to a lack of public disclosure?" The Agency has at it's disposal the data concerning the number of Investigational Device Exemption (IDE) trials being conducted and the number of patients expected to be enrolled. If one assumes that only a device used in an IDE trial could qualify as being to treat "serious or life threatening conditions," the current need for patients is clearly identified.

Many factors go into the rate at which patients are enrolled into device trials. The availability of the device during a clinical trial is typically very controlled by the sponsor. In fact the pace of enrollment is often dictated by the desire of a sponsor to limit their exposure to risks of device problems by limiting the number of devices in distribution. The clinical trial is the time when one expects to uncover problems with the product. Expanding the number of patients put at risk from these problems has a negative health impact.

The other concern such a data bank raises for TCI is the possible incentive to conduct trials where such disclosure is not mandated. This incentive is due to the competitive advantage that will be lost if the proposed data bank is established. The data bank can be used by a potential competitor to glean information regarding future marketing strategy and product development. A competitor can review the public data bank for information on indications for use and learn the target population for future marketing efforts. These competitors can also get a list of the investigational sites to target in efforts to derail the sponsor's clinical trial plans. The risk of these competitive disadvantages must be weighed by sponsors against the benefit of having a clinical trial performed in the United States. If the same trial can be conducted in a country without the need to disclose this information to competitors, the movement of sponsors to off-shore trial sites would deprive the U.S. population of a potential benefit.

Feeding this competitive risk is an expectation the public would have for an update to the data in this data bank as any information changes. Therefore sponsors will be required to continuously submit corrections as study sites are added or indications for use change. Doing this allows a competitor up-to-date information regarding changes in marketing plans or hospital affiliations. Sponsors may find the risk from this early disclosure of critical data to be so large that clinical trials in the U.S. would be limited or eliminated.

Due to these risks to public health and availability of experimental devices, TCI recommends against establishing the proposed data bank. Without any clear presentation of the current unmet need, review of the proposal for adequacy in meeting the need cannot be completed. If the Agency presents further explicit data in support of establishing that a need for such a data bank exists, TCI requests that the comment period be reopened.

Sincerely,

Tim Krauskopf, R.A.C.
Vice President of Regulatory and Clinical Affairs

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